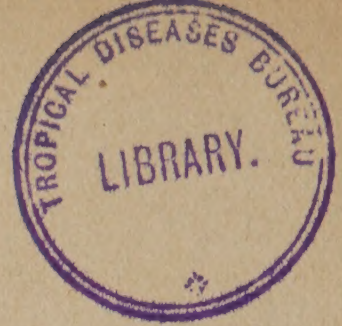


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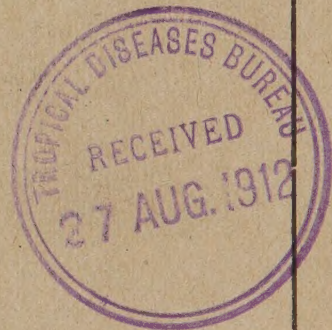


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STUDIES OF MALARIA IN PANAMA: IV. RELATION OF
MALARIA TO OTHER DISEASES WITH
ESPECIAL REFERENCE TO
DYSENTERY *

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This study was begun with the idea of examining data bearing on the so-called dysenteric type of pernicious malarial fever. The study naturally extended itself until it included besides the malarial fevers the six largest groups of disease met with in Panama, namely, acute dysentery, amebic dysentery, typhoid fever, pneumonia, pulmonary tuberculosis and chronic nephritis. The statistics that will be given cover the years 1908 and 1910, during which the records of the hospital are most complete.

Among eighty-eight cases of pernicious malarial fever that occurred in Colon Hospital from November, 1907, to May, 1910, thirteen patients had diarrhea, usually slight, and twenty patients were constipated. The remaining fifty-three patients showed no intestinal disturbance. All patients were given as routine 3 grains of calomel on the evening of admission and 2 ounces of a half saturated solution of magnesium sulphate the following morning. The slight diarrhea noted in a few cases was not in excess of what might be accounted for by the purgatives. It is safe to say that without purgatives a great majority of the patients would have been badly constipated. In not a single instance were there dysenteric phenomena — diarrhea, tenesmus, and stools containing blood and mucus. I have observed, also, many other pernicious cases in Panama which are not included in this series, and I have seen neither the "choleraic" nor "dysenteric" types, although I have watched for them carefully. The intensity of infection in the pernicious cases has varied all the way up to a 66 per cent. infection of the red corpuscles in the peripheral blood.

I may say at once, then, that the "choleraic" and "dysenteric" types of pernicious malarial fever have not occurred in my experience in Panama, and I know of no such cases in the literature in which coincident bacillary dysentery or other intestinal bacterial infections have been excluded by bacteriological examinations of the dysenteric stools. The mere presence of many malarial parasites in the intestinal capillaries of

*From the Medical Clinic of Colon Hospital, Cristobal, Canal Zone.

*Read at the meeting of the Los Angeles County Medical Society, Oct. 20, 1911.

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TABLE I.—CONDITIONS COMPLICATING MALARIAL INFECTIONS BY MONTHS FOR 1908 AND 1910

Date	E. A.*	Ter.†	Acute Dys.	Acute Dys. and E. A.	Acute Dys. and Ter.	Amebic Dys.	Amebic Dys. and E. A.	Amebic Dys. and Ter.	Typhoid	Typhoid and E. A.	Typhoid and Ter.	Pneumonia	Pneumonia and E. A.	Pneumonia and Ter.	Tb. pul.	Tb. and E. A.	Tb. and Ter.	Nephritis chr.	N. and E. A.	N. and Ter.
1908																				
January	132	54	6	1	0	14	2	0	7	0	1	21	1	0	18	1	1	1	1	1
February	74	34	7	4	1	6	1	0	6	1	1	15	0	1	12	5	2	8	1	0
March	62	36	8	2	0	6	0	0	11	1	0	11	1	0	9	1	0	8	0	0
April	84	36	5	0	0	8	2	0	5	0	2	13	0	0	8	0	0	5	1	0
May	42	27	2	1	0	10	0	1	2	1	0	18	1	1	13	0	0	16	1	0
June	66	25	4	0	0	4	0	1	3	1	0	27	1	0	10	0	0	18	1	0
July	354	73	4	0	0	6	1	0	6	0	0	13	2	0	14	1	0	14	3	0
August	402	70	5	1	0	12	1	0	2	0	0	4	1	0	25	2	0	6	0	0
September	321	69	5	1	1	9	4	1	10	1	1	9	1	1	10	2	0	12	4	1
October	526	56	5	3	0	9	4	1	7	1	1	9	1	0	22	4	0	7	1	0
November	279	26	7	3	0	14	9	0	6	4	0	9	2	0	21	4	0	10	4	0
December	147	26	6	2	0	20	4	1	2	2	0	7	1	0	28	9	0	10	5	0
	2,489	532	64	18	1	118	28	5	67	11	6	156	12	3	190	29	3	121	22	3
1910																				
January	44	11	16	2	1	5	0	0	3	1	0	4	1	0	17	1	0	10	1	0
February	30	9	8	1	0	2	0	0	2	0	0	5	0	0	10	0	0	4	0	0
March	29	11	9	0	0	3*	0	0	3	1	0	1	0	0	16	0	0	7	0	0
April	59	18	9	1	0	4	0	0	4	0	1	7	0	0	18	1	0	18	2	0
May	57	12	4	0	0	1	0	0	5	0	0	6	1	0	23	1	0	13	1	1
June	298	43	10	0	1	4	0	0	3	0	0	11	0	0	10	0	0	5	1	0
July	356	34	12	4	0	1	0	0	1	0	0	12	0	0	10	0	0	12	6	0
August	277	38	14	3	0	3	1	0	6	0	0	9	1	0	12	1	0	19	4	0
September	116	40	9	1	1	8	1	0	7	0	0	9	0	0	17	1	0	8	1	0
October	52	17	1	0	0	0	0	0	6	0	0	5	1	0	14	0	0	7	1	0
November	49	6	9	2	0	1	1	0	4	0	0	6	0	0	11	0	0	8	0	0
December	51	13	3	0	0	0	0	0	2	1	0	13	1	0	5	1	0	11	0	0
	1,418	252	104	14	3	32	3	0	46	3	1	88	5	0	163	6	0	122	17	1
Total	3,907	784	168	32	4	150	31	5	113	14	7	244	17	3	353	35	3	243	39	4

*E. A.—Estivo-autumnal malarial parasites.

†Ter.—Tertian.

certain dysenteric patients is not sufficient evidence to prove that the dysentery was of malarial origin. The dysentery itself, as will be shown later, probably tends to cause an exacerbation of a latent malarial infection. Thirty-nine of our eighty-eight patients with pernicious malarial fever died and practically all of them were examined post mortem. In none was there any evidence of enterocolitis.

On the other hand, a small percentage of both estivo-autumnal and tertian malarial infections of mild or moderate intensity have been complicated by acute dysentery. Likewise a small percentage have been complicated by amebic dysentery, typhoid fever, pneumonia, pulmonary tuberculosis and chronic nephritis.

Table 1 represents the number of these complicating infections by months for the years 1908 and 1910. In connection with it, it is interesting to note that during the year 1908, 28.32 per cent. of the employees of the Isthmian Canal Commission were admitted to the hospitals with

TABLE 2.—SHOWING THE PERCENTAGE OF MALARIAL INFECTIONS COMPLICATED BY OTHER DISEASES

	Total	Acute Dysent.		Amebic Dysent.		Typhoid Fever		Pneumonia		Tuberculosis		Nephritis	
	No. Cases	No. Cases	Per cent.	No. Cases	Per cent.	No. Cases	Per cent.	No. Cases	Per cent.	No. Cases	Per cent.	No. Cases	Per cent.
Mal. E. A.	3,907	32	.82	31	.79	14	.36	17	.44	35	.90	39	1.00
Mal. Ter.	784	4	.51	5	.64	7	.89	3	.38	3	.38	4	.51

malarial fever, while during 1910 only 18.6 per cent. were admitted.¹ That is, the number of malarial infections in 1910 was almost exactly two-thirds of the number in 1908. The effect of this difference on the frequency of complications is striking.

For purposes of analysis it is necessary to construct subtables from Table 1.

Malarial infections were complicated by the above diseases in such a small percentage (1 per cent. or less) of instances that it is impossible to think that malaria was concerned with the onset of any of them. Furthermore, there is no striking difference in the relative percentages, as there should be if malaria were an etiologic factor in any one. The percentage of complications by acute dysentery² is practically the same

1. Gorgas, W. C.: Report of the Department of Sanitation of the Isthmian Canal Commission for the month of January, 1911.

2. Recent bacteriological studies conducted at Colon Hospital indicate that most of the cases of acute dysentery are due to *B. dysenteriae* (Shiga and His Y).

as by amebic dysentery. The table does not yield the slightest evidence that malaria predisposes to any of the complicating diseases included in the tables.

TABLE 3.—SHOWING THE PERCENTAGE OF OTHER DISEASES COMPLICATED BY MALARIA

Disease	Total No.	E. A.		Ter.		Corrected Ter.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.
Acute Dysentery	168	32	19.0	4	2.4	20	12.0
Amebic Dysentery	150	31	20.6	5	3.3	25	16.7
Typhoid fever	113	14	12.4	7	6.2	35	31.0
Pneumonia	244	17	7.0	3	1.2	15	6.2
Tuberculosis	353	35	10.0	3	0.9	15	4.2
Nephritis	243	39	16.0	4	1.6	20	8.2

The column “corrected tertian” indicates what would have been the tertian complications if the number of tertian infections (784) had been equal to the number of estivo-autumnal infections (3,907).

In order to interpret Table 3 it is necessary to estimate the chance of coincident infections of malaria and the other diseases. This would be simple, given the population drawn from, if all the infections had occurred at the same time, or if all had continued throughout the two years. For instance, suppose the population drawn from to be 15,000. Of this number 168, or 1.12 per cent., had acute dysentery, and 3,907 had estivo-autumnal malaria. Then 1.12 per cent. of 3,907 would indicate the number of estivo-autumnal infections that would probably be complicated by acute dysentery; that is, about forty-four cases. But all the infections did not occur at the same time. They were distributed, as shown in Table 1, throughout the years 1908 and 1910. In order to obtain the true rate of coincidence, therefore, it is necessary to calculate the chance of synchronous infection for each month in the two years. Table 4 shows how this was done to obtain the number of infections that might be attributed to coincidence in the case of estivo-autumnal malaria and acute dysentery. The population that Colon Hospital drew its patients from in 1909 was approximately 16,000; in 1910, 13,500.

Coincident infections of estivo-autumnal malaria and acute dysentery could be expected, then, in only about two instances. It is unnecessary to present a similar table for each of the diseases studied, but such a table for each has been worked out. The results are given in Table 5.

TABLE 4.—SHOWING CHANCE OF COINCIDENT INFECTIONS OF ESTIVO-AUTUMNAL MALARIA AND ACUTE DYSENTERY

Date, 1908 Population 16,000	Cases of Acute Dysentery	Proportion of Population Having Acute Dysentery	Cases of E. A. Malaria	Number of Coincident Infections Calculated
January	6	.00038	132	.050
February	7	.00044	74	.033
March	8	.00050	62	.031
April	5	.00031	84	.026
May	2	.00013	42	.006
June	4	.00025	66	.017
July	4	.00025	354	.089
August	5	.00031	402	.125
September	5	.00031	321	.099
October	5	.00031	526	.163
November	7	.00044	279	.123
December	6	.00038	147	.056
Total number of coincident infections to be expected in 1908.....				.798
1910, Population 13,500				
January	16	.00119	44	.052
February	8	.00059	30	.018
March	9	.00067	29	.019
April	9	.00067	59	.040
May	4	.00030	57	.017
June	10	.00074	298	.221
July	12	.00089	356	.317
August	14	.00104	277	.288
September	9	.00067	116	.078
October	1	.00007	52	.004
November	9	.00067	49	.032
December	3	.00022	51	.011
Total number of coincident infections to be expected in 1910....				1.097
Total number in 1908 and 1910.....				1.895

TABLE 5.—SHOWING THE CHANCES OF COINCIDENT INFECTIONS OF ESTIVO-AUTUMNAL MALARIA AND OTHER DISEASES IN 3,907 CASES

Complicating Disease	No. of Cases of Complicat- ing Disease	Calculated Coincidence of Infection	Real No. of Synchronous Infections
Acute dysentery	168	1.895	32
Amebic dysentery	150	1.888	31
Typhoid fever	113	1.295	14
Pneumonia	244	2.484	17
Tuberculosis	353	4.135	35
Nephritis	243	2.646	39

This table is not exactly accurate. It assumes that the infections of each month occurred at the same time during the month or that each infection lasted throughout the month. This is an assumption, of course, not strictly true, especially in the chronic diseases, tuberculosis and nephritis, which, for purposes of discussion, may be assumed to last a year. Calculating from this as a basis, the number of coincident infections of estivo-autumnal malaria with tuberculosis would be about forty-nine; with chronic nephritis, about thirty. The calculated number of coincident infections of estivo-autumnal malaria with tuberculosis and nephritis approximately equals the real number of synchronous infections, if I may use the word "infection" in connection with nephritis.

But the real number of synchronous infections with the other four diseases cannot be accounted for by chance. That malaria cannot be held responsible for the onset of any of the diseases has been shown by a study of the pernicious malarial cases and by Table 2. The alternative is that the diseases, acute dysentery, amebic dysentery, typhoid fever and pneumonia, cause an exacerbation of latent malarial infections, and this is probably the true explanation. A large proportion of the population served by Colon Hospital has had malaria, and we may infer from our knowledge of malaria that in a considerable percentage of patients the infection was not entirely eradicated; that is, they still had a latent malarial infection. If it is assumed that 18 per cent. of the population had latent malaria, then 18 per cent. of the 168 acute dysentery cases, or thirty infections, would be superimposed on latent malaria.³ If these thirty latent malarial infections were "lighted up" by the dysentery, and if one adds to them the two cases of calculated coincident infections, the number thirty-two is obtained, which is the exact number of real synchronous infections. Of course, this calculation is too exact to represent the truth of the matter, but I think that it indicates the true explanation of the combinations of malaria and the other diseases in Panama.

If the explanation is correct, the interpretation of Tables 3 and 5 is clear. Four of the diseases studied have a tendency to cause an exacerbation of latent malarial infections, and in the following order: amebic dysentery, acute dysentery, typhoid fever, lobar pneumonia. In the discussion following Table 5 it is concluded that tuberculosis and chronic nephritis probably do not have such a tendency, and that the synchronous infections can be accounted for by coincidence.

3. During the dry season of 1909, Darling determined the latent malarial rate in villages where no anopheles were breeding. He found that 10 per cent. of men who were at work without symptoms had parasites. Among the families of Spanish and West Indian laborers the rate was 30 per cent. The latent malarial rate taken the year around must be much larger than Darling found it during the dry season, and 18 per cent. seems a conservative estimate. (Darling, S. T.: *Jour. Amer. Med. Assn.*, 1909, liii, 2051.)

It is probable that this marked tendency of the dysenteries, causing a high rate of synchronous infection, furnishes an explanation of the common belief that malaria may itself cause dysenteric phenomena. The effect has probably been mistaken for the cause.

Additional evidence against the malarial origin of acute dysentery is found when one examines Table 1 by months. In 1908, when the malarial rate was high, the total number of cases of acute dysentery was only sixty-four, and 28 per cent. of the cases were complicated by estivo-autumnal malaria. On the other hand, in 1910 when the malarial rate was only two-thirds as high, the number of cases of acute dysentery was 104, or two-thirds greater, and there were estivo-autumnal infections in only 13.4 per cent. of the cases. The number of cases of acute dysentery bears no relation, therefore, to the malarial rate, but the number of instances in which acute dysentery was complicated by malaria is in direct relation to the malarial rate, and, presumably, to the number of latent malarial infections.

After the preceding part of this paper was written a patient with an estivo-autumnal infection was admitted to the hospital. On the fifth day, when his temperature had reached normal, there was a sharp secondary rise and on the sixth day a sharp dysentery developed with pus, blood and mucus in the stools. We immediately made cultures on Endo's medium, from which we isolated *B. dysenteriae* (His Y). This case was evidently one of the rare instances of coincident infection due to chance, for the dysentery did not precede the malarial fever and cause an exacerbation of a latent infection, but it developed at the beginning of malarial convalescence. The dysentery subsided and the temperature was normal within three days. This might easily have been considered an attack of malarial dysentery if cultures had not been made.

CONCLUSIONS AND SUMMARY

1. The so-called "choleraic" and "dysenteric" types of pernicious malarial fever do not occur in Panama.

2. In a study of 4,691 malarial infections it was found that the number of cases complicated by acute dysentery, amebic dysentery, typhoid fever, pneumonia, pulmonary tuberculosis, and chronic nephritis was in each instance 1 per cent. or less.

3. Malarial infection appears to bear no etiologic relationship to acute dysentery or any of the above diseases.

4. All the above diseases were complicated by a considerable percentage of malarial infections, the order of frequency being amebic dysentery, acute dysentery, chronic nephritis, typhoid fever, pulmonary tuberculosis, pneumonia.

5. It is shown that the coincident occurrence of malaria with nephritis and tuberculosis is probably due to chance, while the synchronous

occurrence of malaria with acute dysentery, amebic dysentery, typhoid fever and pneumonia is chiefly due to a "lighting up" of latent malaria by the other diseases. The two forms of dysentery have about equal power to determine an exacerbation of latent malaria; the influence of typhoid fever and pneumonia is only about one-third or one-fourth as great.

I wish to thank Col. W. C. Gorgas, Chief Sanitary Officer of the Canal Zone, for permission to use the material on which this paper is based.

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